03/04/05

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TRANSMITTAL OF APPEAL BRIEF	Docket No. H1890.0201

In re Application of: Gary D. Hodgen et al.

Application No.	Filing Date	Examiner	Group Art Unit
09/313,628	May 18, 1999	R. S. Travers	1617

Invention: CONTROL OF SELECTIVE ESTROGEN RECEPTOR MODULATORS

TO THE COMMISSIONER OF PATENTS:

Transmitted herewith is the Appeal Brief in this application, with respect to the Notice of Appeal filed: December 30, 2004 .

The fee for filing this Appeal Brief is $ 250.00 .

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☐ A petition for extension of time is also enclosed.

The fee for the extension of time is _____ .

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☒ The Director is hereby authorized to charge any additional fees that may be required or credit any overpayment to Deposit Account No. 50-2215 .
This sheet is submitted in duplicate.

Edward A. Meilman

Dated: March 3, 2005

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Dated: March 3, 2005 Signature: Edward A. Meilman (Edward A. Meilman)

Application No. (if known): 09/313,628 Attorney Docket No.: H1890.0201

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Appeal Brief - In triplicate
Transmittal of Appeal Brief
Fee Transmittal
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Effective on 12/08/2004.
Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).

FEE TRANSMITTAL
For FY 2005

[X] Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 250.00

Complete if Known	
Application Number	09/313,628
Filing Date	May 18, 1999
First Named Inventor	Gary D. Hodgen
Examiner Name	R. S. Travers
Art Unit	1617
Attorney Docket No.	H1890.0201

METHOD OF PAYMENT (check all that apply)

[ ] Check [X] Credit Card [ ] Money Order [ ] None [ ] Other (please identify): _____

[ ] Deposit Account Deposit Account Number: 50-2215 Deposit Account Name: Dickstein Shapiro Morin & Oshinsky LLP

For the above-identified deposit account, the Director is hereby authorized to: (check all that apply)

[ ] Charge fee(s) indicated below
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[X] Credit any overpayments

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES

	FILING FEES		SEARCH FEES		EXAMINATION FEES		
Application Type	**Fee ($)**	**Small Entity Fee ($)**	**Fee ($)**	**Small Entity Fee ($)**	**Fee ($)**	**Small Entity Fee ($)**	**Fees Paid ($)**
Utility	300	150	500	250	200	100	
Design	200	100	100	50	130	65	
Plant	200	100	300	150	160	80	
Reissue	300	150	500	250	600	300	
Provisional	200	100	0	0	0	0	

2. EXCESS CLAIM FEES

Fee Description	**Fee ($)**	**Small Entity Fee ($)**
Each claim over 20 (including Reissues)	50	25
Each independent claim over 3 (including Reissues)	200	100
Multiple dependent claims	360	180

Total Claims		**Extra Claims**	**Fee ($)**	**Fee Paid ($)**
_____	- =	_____	x _____	= _____

Multiple Dependent Claims

Fee ($)	**Fee Paid ($)**
_____	_____

Indep. Claims		**Extra Claims**	**Fee ($)**	**Fee Paid ($)**
_____	- =	_____	x _____	= _____

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets		**Extra Sheets**		**Number of each additional 50 or fraction thereof**	**Fee ($)**	**Fee Paid ($)**
_____	- 100 =	_____	/50	_____ (round up to a whole number) x	_____	= _____

4. OTHER FEE(S) **Fees Paid ($)**

Non-English Specification, $130 fee (no small entity discount)

Other (e.g., late filing surcharge): 2402 Filing a brief in support of an appeal 250.00

SUBMITTED BY

Signature	Edward A. Meilman	Registration No. (Attorney/Agent)	24,735	Telephone	(212) 896-5471
Name (Print/Type)	Edward A. Meilman			Date	March 3, 2005

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Dated: 3/3/05 Signature: Edward A. Meilman (Edward A. Meilman)

Docket No.: H1890.0201
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:

Gary D. Hodgen et al.

Application No.: 09/313,628

Filed: May 18, 1999

Art Unit: 1617

For: CONTROL OF SELECTIVE ESTROGEN RECEPTOR MODULATORS

Examiner: R. S. Travers

APPEAL BRIEF

MS Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

As required under § 41.37(a), this brief is filed within two months after the Notice of Appeal filed in this case on January 3, 2005, and is in furtherance of said Notice of Appeal.

This brief contains items under the following headings as required by 37 C.F.R. § 41.37 and M.P.E.P. § 1206:

I.	Real Party In Interest
II	Related Appeals and Interferences
III.	Status of Claims
IV.	Status of Amendments
V.	Summary of Claimed Subject Matter
VI.	Grounds of Rejection to be Reviewed on Appeal

I. REAL PARTY IN INTEREST

The real party in interest for this appeal is:

Eastern Virginia Medical School (by change of name from Medical College of Hampton Roads).

II. RELATED APPEALS, INTERFERENCES, AND JUDICIAL PROCEEDINGS

There are no other appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

III. STATUS OF CLAIMS

Total Number of Claims in Application: 23

Current Status of Claims

Claims canceled: 1-20

Claims withdrawn from consideration but not canceled: 34-43

Claims rejected: 21-33

Claims On Appeal

The claims on appeal are claims 21-33

IV. STATUS OF AMENDMENTS

Applicant did not amend the claims after Final Rejection.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The use of estrogen for contraceptive purposes is well known, as is the undesirable bleeding side effect of estrogen treatments. To overcome this problem, use of a Selective Estrogen Receptor Modulator (also known as a "SERM") was proposed. However, while SERM treatment was found to obviate the bleeding problem for a short period of time, the estrogen bleeding side effect was found to reappear and, in addition, the administration was found to be fertility inducing rather than contraceptive.

The present invention is based on the discovery that there is an amount of progestogenic agent which is effective to modulate the bleeding side-effect of the SERM and at the same time, permit the SERM to be used for contraceptive purposes.

VI. GROUNDS OF OBJECTION TO BE REVIEWED ON APPEAL

Claims 21-33 were rejected under 35 U.S.C. § 103 as being allegedly unpatentable over *Jones et al.* (U.S. Patent No. 4,133,814; "*Jones*"); *Basu* (*Jap. J. Exp. Med.*, 1973, 43(1):9-15; "*Basu*"); *Shane et al.* (*Fertil. Steril.*, 1978, 29(6):692-4; "*Shane*"), in view of *Merck Manual*.

VII. ARGUMENT

The use of estrogen for a variety of purposes, including contraception, is known. For example, the most prevalent form of oral contraceptive is a pill combining estrogen with progestin.

Despite their value, estrogen treatments are associated with undesirable side effects such as endometrial cancer and bleeding. To overcome these problems, a variety of alternatives have been tried. One was the use of a Selective Estrogen Receptor Modulator (also known as a "SERM"), which compete for the body's estrogen receptor and reduce the production of endogenous estrogen. However, it was found that the body's mechanisms are such that at a point in time, which is totally unpredictable and which varies from individual to individual, the SERM actual causes endogenous production of estrogen. The resulting "run away" estrogen concentration can induce ovulation in those situations where the SERM administration was designed to provide contraception.

Another undesirable side-effect of estrogen treatments is bleeding and it was found that while a SERM treatment will obviate that problem for a short period of time, the estrogen side effects reappear due to the overproduction of endogenous estrogen by the body.

The present invention is designed to modulate the side-effects of the of the SERM and to do so, used is an agent which exhibits progestogenic activity. Such agents have their own side effects when used for contraceptive purposes, which most particularly include the side effect of severe breakthrough bleeding. The present invention is based on the discovery that there is an amount of progestogenic agent which is effective to modulate the bleeding side effect of the SERM and at the same time, permit the SERM to be used for contraceptive purposes.

The rejection on appeal is based on a combination of Jones, Basu, Shane and the Merck Manual. The combination is inappropriate and even if made, does not teach or suggest the claimed invention.

The Jones and Basu references have been cited to show the use of SERMs in connection with contraception. While nether deals with humans, applicants acknowledge they reflect the early beliefs about SERMs. However, it later became apparent that in humans, SERMs were actually fertility agents, rather than contraceptive agents. See Clark, of record, and Greenblat (demonstrating that the SERM clomiphene (MRL 41) induced ovulation and discussing the contrast between rats and women), also of record. Since the SERM causes "run away" endogenous estrogen production, which induces ovulation in addition to exaggerating the estrogen caused bleeding side effect, use of a SERM for contraception was, at the time of the present invention, contraindicated.

Shane has been cited to show a particular progestin as an oral contraceptive. In the human female, however, it is well known that progestins induce bleeding. The Merck Manuel confirms this fact.

The present invention is based on the discovery that there is an amount of progestogenic agent which is effective to modulate the bleeding side effect of the SERM and at the same time, permit the SERM to be used for contraceptive purposes. It is the applicants' position that use of the combination as claimed is unobvious, particularly since it makes no sense to combine the use of an agent which induces bleeding with use of a material known to have a bleeding side effect. The finding that there is an amount of progestin which can be used to modulate the SERM bleeding problem is unexpected. The ability to use the SERM so modified for contraceptive purposes is also unexpected.

The Examiner has acknowledged that the references fail to teach or suggest the concomitant employment of the two agents, the administration levels, and bleeding amelioration. To overcome these deficiencies, three arguments are advanced (see the Advisory Action).

First, it is argued that it is obvious to combine compounds each of which is taught by the prior art to be useful for the same purpose, in order to form a composition which is to be used for the very same purpose. This argument is wrong because it not only presupposes that a composition is being claimed, but it also assumes that it was known to use progestogenic agent to effect the bleeding side effect of the SERM. But a method is being claimed and there is nothing in the record to suggest that it was known any progestogenic agent would effect the bleeding side effect of the SERM in any way. Indeed, of women receiving progestin only contraception, about one-third stop because of unwanted bleeding. If anything, any hypothetical concomitant use would be expected to exaggerate the bleeding problem. That contraindicates use of the combination. Thus, there is no factual basis for an essential part of the reasoning underlying the rejection being reviewed in this appeal.

Second, it is argued the claims are to a method of achieving contraception, not ameliorating the bleeding side effect of the SERM. This argument is also wrong because it ignores what the claims on appeal cover. While a method of contraception is being claimed, the claims also specifically recite the use the progestogenic agent in an amount effective to ameliorate or eliminate the bleeding side effect of the SERM. Thus, the amelioration of the bleeding side effect of the SERM is a specific feature of the claims and cannot be ignored. Parenthetically, pending claims 34-43 were withdrawn on the same basis as this argument, and that withdrawal is, for the same reasons, wrong.

Finally, it is asserted that "bleeding is a normal side effect of oral contraceptives." This is a non-sequitur. It is meaningless in the context of the invention. Ameliorating the normal bleeding side effect of oral contraceptives is obviously a desirable objective. Nothing in the prior art suggests how this objective can be achieved.

The prior art rejection being considered in this appeal is clearly based on speculation in the face of an absence of a factual basis. For instance, observing that methods of contraception have been occasioned by bleeding may inherently provide a reason for "something" to be done, it does not provide any factual basis for what should be done, much less what is being done in the present invention.

At best, all of cited prior art references merely teach the use of the disclosed compounds for contraceptive purposes, but even that requires ignoring the state of the art in that those skilled in this art moved from considering SERMs as contraceptive agents to being fertility (anti-contraceptive) agents between the date of the references and the date of the present invention. The references do not teach or even suggest, either alone or in combination, an improvement in the use of the compounds or methods of ameliorating or eliminating side effects, such as uterine bleeding, that accompany any (presumptive) contraceptive use of SERMs. None of the references motivates one skilled in the art to combine them to realize the invention recited in the claims on appeal.

In light of all of the foregoing considerations, it is respectfully submitted that the rejection under 35 U.S.C. § 103 should be reversed.

VIII. CLAIMS

A copy of the claims involved in the present appeal is attached hereto as Appendix A.

IX. EVIDENCE

No evidence pursuant to §§ 1.130, 1.131, or 1.132 or entered by or relied upon by the examiner is being submitted.

X. RELATED PROCEEDINGS

No related proceedings are referenced in II. above, or copies of decisions in related proceedings are not provided, hence no Appendix thereof is included.

Dated: March 2, 2005

Respectfully submitted,

By 

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APPENDIX A

Claims Involved in the Appeal of Application Serial No. 09/313,628

21. In a method of achieving contraception in a premenopausal human female by administering to the female a contraception effective amount of a contraceptive agent, the improvement which comprises said agent being a combination of a contraception effective amount of a Selective Estrogen Receptor Modulator and an agent which exhibits progestogenic activity, wherein the amount of the agent which exhibits progestogenic activity is effective to ameliorate or eliminate the bleeding side effects of the Selective Estrogen Receptor Modulator.

22. The method of claim 21 wherein the Selective Estrogen Receptor Modulator is clomiphene.

23. The method of claim 21 wherein the Selective Estrogen Receptor Modulator is a benzothiophene.

24. The method of claim 21 wherein the agent which exhibits progestogenic activity is an antiprogestin.

25. The method of claim 24 wherein the antiprogestin is a progesterone receptor antagonist.

26. The method of claim 25 wherein the Selective Estrogen Receptor Modulator is clomiphene.

27. The method of claim 25 wherein the Selective Estrogen Receptor Modulator is a benzothiophene.

28. The method of claim 24 wherein the amount of antiprogestin is that sufficient to maintain the blood estrogen concentration in the range of about 25 to 125 pg/ml.

29. The method of claim 28 wherein the amount of antiprogestin is that sufficient to maintain the blood estrogen concentration in the range of about 60 to 90 pg/ml.

30. The method of claim 21 wherein the agent which exhibits progestogenic activity expresses both androgenic and progestogenic activity.

31. The method of claim 30 wherein the agent which exhibits progestogenic activity comprises the combination of an androgen and a progestin.

32. The method of claim 30 wherein the agent which exhibits progestogenic activity is a single material which expresses both activities.

33. The method of claim 32 wherein the agent which exhibits progestogenic activity is danazol or levonorgestrel.

34. (Withdrawn) A method of ameliorating or eliminating dysfunctional uterine bleeding that accompanies contraceptive administration of a Selective Estrogen Receptor Modulator (SERM) to a female receiving contraception, comprising coadministering with the SERM to said subject an ameliorating or eliminating dysfunctional uterine bleeding effective amount of an agent that exhibits progestogenic activity.

35. (Withdrawn) The method of claim 34, wherein the agent that exhibits progestogenic activity also exhibits androgenic activity.

36. (Withdrawn)The method of claim 34, wherein said SERM is clomiphene, tamoxifen, or a benzothiophene or a pharmaceutically acceptable salt or complex thereof.

37. (Withdrawn)The method of claim 35, wherein said SERM is clomiphene, tamoxifen, or a benzothiophene or a pharmaceutically acceptable salt or complex thereof.

38. (Withdrawn)The method of claim 34, wherein said progestogenically active compound is progesterone, levonorgestrel, danazol, or medroxprogesterone acetate.

39. (Withdrawn)The method of claim 36, wherein said progestogenically active compound is progesterone, levonorgestrel, danazol, or medroxprogesterone acetate.

40. (Withdrawn)The method of claim 34, wherein said effective amount of the progestogenically active compound is sufficient to maintain a blood level of endogenous estrogen in the range of about 25 to 125 pg/ml.

41. (Withdrawn)The method of claim 40, wherein said blood level is in the range of about 60 to 90 pg/ml.

42. (Withdrawn)The method of claim 34, wherein said progestogenically active compound is coadministered to said subject with an androgenically active compound.

43. (Withdrawn)The method of claim 42, wherein said androgenically active compound is testosterone.